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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,343	04/11/2005	Jacques Mallet	BJS-3665-122	3751

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,343	MALLET ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,36 and 43-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35, 36 and 43-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Applicants' response of May 11, 2007, to the non-final action dated November 14, 2006 has been entered. Claims 35, 36 and 43-67 are pending in the application. Claims 35, 43-46, 53, 54, 58 and 64-67 have been amended. No claims have been cancelled or newly added. Claims 35, 36 and 43-67 are currently under examination.

Response to Claim Objections

Claims 43-46 were objected to as depending from canceled claims 38 and 39, in the previous office action dated November 14, 2006. In view of Applicants' amendment of claim 43-46, to depend from pending claim 35, the previous objection is hereby withdrawn.

Response to Claim Rejections - 35 USC § 112- Second Paragraph

Claims 43-46 and 53-56 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite, in the previous office action dated November 14, 2006. In view of Applicants' amendment of claim 43-46, to depend from pending claim 35, and amendment of claims 53 and 54 directing the claims to a recombinant cell and a composition comprising a vector, the previous rejections are hereby withdrawn.

Response to Claim Rejections - 35 USC § 112, Written Description

Claims 36, 38-39, 43-56, 58 and 64-67 stand rejected under 35 U.S.C.§112, first paragraph, as failing to comply with the written description requirement. In view of Applicants' amendment of base claim 35, deleting language directed to a functional portion of a UTR region, the rejection of claim 35, 36, 47-56 and 58 is hereby withdrawn. The rejection set forth on pp. 3-4 of the previous office action dated November 14, 2006 is maintained for claims 43-46, and 64-67, for reasons of record.

Applicants argue that the claims are believed to be supported by an adequate written description because one of ordinary skill will appreciate the applicants were in possession of the

claimed invention, and that the specification teaches how to use the claimed invention, without requiring recitation of specific posttranscriptional regulatory sequences, as the description explains that the functions of these sequences were known in the art. Applicants' arguments have been fully considered, but not found persuasive.

As was indicted in the previous office action, the claims encompass numerous polynucleotide sequences comprising portions or fragments of numerous posttranscriptional regulatory elements that retain functional activity. The recitation of posttranscriptional regulatory elements comprising a functional portion of a UTR does not provide an adequate written description for said functional portion because the neither the prior art nor the specification provides examples of functional portions or functional fragments of the disclosed sequences (SEQ ID NOS: 1-4) which demonstrate that such fragments of regulatory sequences would actually retain posttranscriptional, promoter or mRNA stabilization functions.

Therefore, the rejection of claims 43-46, and 64-67, is maintained for reasons of record and the foregoing discussion.

Response to Claim Rejections - 35 USC § 112-Scope of Enablement

Claims 35, 36, 43-56, 58 and 64-67 stand rejected under 35 U.S.C. §112, first paragraph, because the specification does not reasonably provide an enablement for the full scope of the invention. In view of Applicants' amendment of base claim 35, deleting language directed to a portion of a UTR region, the rejection of claim 36, 47-56 and 58 is hereby withdrawn. The rejection set forth on p. 4 of the previous office action dated November 14, 2006 is maintained for claims 35, 43-46, 54-56 and 64-67, for reasons of record.

Applicants argue that amended claim 35 now specifies that the vector is suitable for *in vitro* transgene delivery into mammalian cells, and the amended method claims require an *in vitro* or *ex vivo* expression of a transgene. Further stating that the Examiner has acknowledged that the specification is enabling for a vector comprising a transgene operably linked to at least two distinct posttranscriptional regulatory elements comprising UTR regions selected from WPRE, APP, tau and TH elements suitable for transgene delivery to mammalian cells, and methods for expressing a transgene in mammalian cells *in vitro*, using said vector.

Applicants arguments have been fully considered, but not found persuasive. As was indicted in the previous office action, the specification is not enabling for the broad family of vectors (that include a plasmid, a recombinant virus, a cosmid, an artificial chromosome, an episome etc.) comprising portions or functional fragments of posttranscriptional regulatory elements as gene therapy compositions for treating human disease that include retinal degenerative disease, or methods comprising expressing a transgene encoded by said vectors in fibroblasts and neuronal cells *in vivo.* Applicants' amendment of base claim 54 to recite a composition comprising a vector **suitable** for *in vitro* transgene delivery into mammalian cells or a recombinant cell comprising the same fails to obviate the rejection, because a vector suitable for *in vitro* delivery does not preclude its use for *in vivo* delivery. Moreover, the composition further comprises a pharmaceutically acceptable carrier or excipient and is used to treat a human disease by gene therapy or cell therapy.

Therefore, the rejection of claims 35, 43-46, 54-56 and 64-67, is maintained for reasons of record and the foregoing discussion.

Response to Claim Rejections - 35 USC § 102

Claims 53-56 were previously rejected under 35 USC § 102(e) as being anticipated by Barsov et al. (U.S. Patent Publication No.: 2002/0110896; filed Sep. 24, 2001), in the office action dated November 14, 2006. In view of Applicants' amendment of claims 53 and 54 to include new limitations that include a vector comprising a transgene operably linked to at least two distinct posttranscriptional regulatory elements selected from a WPRE element, tau 3'UTR, TH3'UTR and APP5'UTR, obviating the ground of rejection, the previous rejection of claims 53-56 is hereby withdrawn.

Response and New Claim Rejections - 35 USC § 103

Claims 35, 36 and 46 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view of Paulding et al. (J. Biol. Chem. 274:2532-2538; of record). Claim 43 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view of Paulding et al.

(J. Biol. Chem. 274:2532-2538; of record), and further in view of Ramezani et al. (Mol. Ther. 2:458-469; 2000; of record). Claims 40, 44, and 64-65 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view of Paulding et al. (J. Biol. Chem. 274:2532-2538; of record) and Ramezani et al. (Mol. Ther. 2:458-469; 2000; of record), and further in view of Rogers et al. (J. Biol. Chem. 274:6421-6431; 1999; of record). Claims 41-42, 45-51, and 66-67 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view Paulding et al. (J. Biol. Chem. 274:2532-2538; of record) and Ramezani et al. (Mol. Ther. 2:458-469; 2000; of record), and Rogers et al. (J. Biol. Chem. 274:6421-6431; 1999; of record), and further in view of Aronov et al. (J. Mol. Nerurosci., 12:131-145; 1999; of record). Claims 52, 56 and 59 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Barry et al. (Hum. Gene Ther. 12:1103-1108; 2001), in view of Chang et al. (Curr. Gene Ther. 2:237-251; 2001).

The rejections set forth on pp. 6-8 of the previous office action dated November 14, 2006 are all maintained over claims 35, 36, and 43-67 for reasons of record.

Applicant's arguments concern the teachings of Barry, the primary reference shared by all the rejections set forth above. Applicants have traversed these rejections and state that Barry does not describe a vector wherein each of the two distinct posttranscriptional regulatory elements comprises a UTR region of a eukaryotic mRNA selected from a WPRE element, tau 3'UTR, TH3'UTR and APP5'UTR. Further stating that the inventors have tested combinations of these posttranscriptional regulatory elements and unexpectedly found that they could cooperate or synergize to provide positive effects on transgene expression, that is not taught by the cited prior art; and the secondary references are not believed to cure these deficiencies. Applicants' arguments have been fully considered, but not found persuasive.

As was indicated in the previous office action of November 14, 2006, Barry et al. describe the generation of lentivirus vectors by combining several posttranscriptional regulatory elements that synergistically increase transgene expression. Barry et al. teach lentiviral vectors for provirus integration into nondividing mammalian cells, wherein the incorporation of two distinct posttranscriptional regulatory elements, namely a central polypurine tract (cPPT) and a human hepatitis virus posttranscriptional regulatory element (PRE; closely related to WPRE), that provide increased transgene expression in mammalian cells, and further provide the

motivation to include two distinct posttranscriptional regulatory sequences, or to substitute or combine additional posttranscriptional regulatory elements with their vector, to increase transduction and stabilize virus vector mRNA for increased transgene expression (first column, p. 1104). The instantly claimed UTR elements are described in the secondary references, where their presence in the vector leads to increased transgene expression. As Barry et al. describe the synergistic effects obtained by combining two distinct posttranascriptional regulatory elements, it would have been obvious for a person of ordinary skill in the art to substitute any of the known UTR elements for the posttranscriptional regulatory element of Barry et al. (PRE) with a reasonable expectation of success.

It should therefore be noted that each of the claimed posttranscriptional regulatory elements comprising a UTR region and their respective functions was known in the prior art (as stated in the instant specification and admitted on the record by Applicants). That the combination of two posttranscriptional regulatory elements in a single vector encoding a transgene would synergistically increase transgene expression was taught by Barry et al. Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention by Applicants to combine any two of the known elements in a single vector, which amounts to simple substitution of one known element for another to yield predictable results. Applicants should further note that the *KSR* case forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR International Co. v. Teleflex Inc.*, 550 U.S.-, 82USPQ2d 1385 (2007).

Therefore, the grounds for rejection of claims 35, 36, and 43-67 are maintained for reasons of record and the foregoing discussion.

Conclusion

Claims 35, 36 and 43-67 are not allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

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